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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/618,579	07/18/00	SELIFONOV	S 02-028950US

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LAW OFFICES OF JONATHAN ALAN QUINE
P O BOX 458
ALAMEDA CA 94501

EXAMINER	
ZHOU,S	
ART UNIT	**PAPER NUMBER**
1631	8

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application r pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/618,579	Applicant(s) SELIFONOV ET AL.	
	Examiner Shubo "Joe" Zhou	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-105 is/are pending in the application.

4a) Of the above claim(s) 1-92 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 93-105 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-105 are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5-7 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

Restriction/Election Requirement

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-46, drawn to methods for making recombinant nucleic acids, classified in Class 435, subclass 91.52. If this group is elected, then the below summarized added specie election is also required.

II. Claims 47-57, drawn to methods of making character strings and a library of recombinant nucleic acids made thereby, classified in Class 435, subclass 91.2 and Class 536, subclass 23.1.

III. Claims 58-61, drawn to methods of facilitating recombination between two ore more divergent nucleic acids and product made thereby, classified in Class 435, subclass 440.

IV. Claims 62-65, drawn to methods of generating and recombining nucleic acids, classified in Class 435, subclass 91.1.

V. Claims 66-74, drawn to methods of optimizing activity of a nucleic acid, classified in Class 435, subclass 6. If this group is elected, then the below summarized added specie election is also required.

VI. Claims 75-81, drawn to methods of providing a library of recombinant nucleic acids which is enriched for a sequence of interest, classified in Class 435, subclass 91.5. If this group is elected, then the below summarized added specie election is also required.

VII. Claims 82-87, drawn to methods of generating a library of biological polymers, classified in Class 436, subclass 536, and Class 435, subclass 69.1. If this group is elected, then the below summarized added specie election is also required.

VIII. Claims 88-92, drawn to an integrated system, classified in Class 702, subclass 19. If this group is elected, then the below summarized added specie election is also required.

IX. Claims 93-105, drawn to methods of producing recombinant nucleic acids or polypeptides involving in silico procedures, classified in Class 702, subclass 19.

The inventions are independent/distinct, each from the other because of the following reasons:

The inventions of Groups (I-VII, and IX) and Group VIII are independent inventions because they are directed to patentably distinct subject matter regarding the critical limitations therein. For Groups (I-VII, and IX), the critical feature is nucleic acids or polypeptides; for Group VIII, the critical feature is an integrated system.

Each of Groups (I-VII, and IX) is directed to a distinct invention. Group I is directed to methods for making recombinant nucleic acids, Group II is directed to methods of making character strings, Group III is directed to methods of facilitating recombination between two ore more divergent nucleic acids, Group IV is directed to methods of generating and recombining nucleic acids, Group V is directed to methods of optimizing the activity of a nucleic acid, Group VI is directed to methods of providing a library of recombinant nucleic acids which is enriched for a sequence of interest, Group VII is directed to methods of generating a library of biological polymers, and Group IX is directed to methods of producing recombinant nucleic acids or polypeptides involving in silico procedures. These methods are distinct both physically and functionally, require

different process steps, reagents and parameters, and produce different products. Consequently, these inventions have acquired a separate status in the art as a separate subject for inventive effect and are usually published separately. The search for each of the above inventions is not co-extensive particularly with regard to the literature search.

Additional Specie election only regarding an election of Group I, V, VI, VII, and VIII above:

It is noted that some claims in the instant application contain multiple species of inventions which require restriction/election.

Claim 6 of Group I is directed to a method of making a recombinant nucleic acid, said method having limitation selected from a group of genetic operators of 14 kinds: starting from page 81, line 26, "a mutation of..." to page 82, line 12, "death of...". This list of genetic operators are considered as species subject matter. These different genetic operators are usually published separately and require different searches. Applicant is required to elect only one species for the claimed invention of Claim 6 in Group I, from the group of 14 species listed above (designated as by the Examiner Species 6-1 ("a mutation of..." on page 81, line 26) through Species 6-14 ("death of..." on page 82, line 12) for the purpose of examination.

Similarly, Claim 92 is directed to an integrated system having limitation selected from a group of genetic operators of 13 kinds: starting from page 108, line 11, "a mutation", to line 15 of the same page, "death". For the same reasons stated above, applicant is required to elect only one species for the claimed invention of Claim 92 in Group VIII, from the group of 13 species listed above (designated as by the Examiner Species 92-1 ("a mutation") through Species 92-13 ("death") for the purpose of examination.

Claim 66 of Group V is directed to method of optimizing activity of a nucleic acid, containing limitations including both nucleic acid and protein, two distinct chemical groups. Applicant is required to elect only one species, either Species 66-1 (nucleic acid) or Species 66-2 (protein) for the purpose of examination.

Claim 78 of Group VI is directed to method of providing a library of recombinant nucleic acids, containing limitations including both a column matrix material and a nucleic acid chip, two distinct species both chemically and physically. Applicant is required to elect only one species, either 78-1 (column matrix material) or 78-2 (nucleic acid chip) for the purpose of examination.

Claim 84 of Group VII is directed to method of generating a library of biological polymers, containing limitations including nucleic acids, polypeptides and peptide nucleic acids, three distinct species. Applicant is required to elect only one species, either 84-1 (nucleic acid), or 84-2 (polypeptide) or 84-3 (peptide nucleic acid) for the purpose of examination.

Because these inventions are independent/distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Jonathan Quine on 4/11/01, a provisional election was made with traverse to prosecute the invention of Group IX, claims 93-105. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-92 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The specification is objected to because of the following:

The abstract has multiple titles, which makes the abstract be composed of more than one paragraphs. See MPEP section 608.01(b).

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at page 73 and elsewhere. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

Appropriate correction is required.

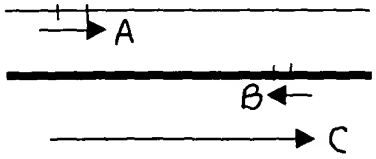
Claim Rejections-35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 94 and 95 are rejected under 35 U.S.C. 112 , second paragraph, as being vague, indefinite and confusing for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrases "bridge" or "bridging" and "correspond" in claims 94 and 95 are confusing. It is unclear what is meant by bridging oligonucleotides that correspond to the crossover sites. There could be several different explanations for bridging oligonucleotides that correspond to crossover sites.



As shown in the above cartoon diagram, the two lines wihtout arrows repsent two parental nucleic acids and the three lines with arrows represent three possible oligonucleotides. The short lines on the parental nucleic acids represent crossover sites. It can be seen that the oligos can either bridge crossover sites like A and B, or bridge two parental nucleic acids corresponding to crossover sites like C, and there could be other explanations.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jonsson et al. (Nucleic Acids Research, 1993, Vol. 21, No.3, pages 733-739).

Jonsson et al. disclose a process and model of analyzing and predicting promoter sequences comprising providing 25 parental nucleic acid sequences (see page 734, Table 1); analyzing the effect of each position on the overall promoter strength (page 735); selecting cross-over sites according to the analysis and determining sequences containing the essence of the structural features characteristic of strong promoters (page 735, first paragraph); selecting two sequences that are predicted to have strong promoter activity in silico, Pls1 and Pls2 (see page 736, left column, and the bottom two sequences of Table 1 at page 734); and synthesizing the two promoter sequences (page 736, right column). Although Jonsson et al. do not explicitly use the term "recombination" or "recombinant" as required in the instant claims, it would have been obvious to one of ordinary skill in the art to have understood that the sequences predicted by the model, Pls1 and Pls2 , are recombinant sequences since they recombine all the sequences of positions in the 25 promoters that contribute most to the maximum overall promoter activity. While Jonsson et al. do not also explicitly disclose the modeling process is done in silico, i.e. using a computer, it would have been obvious to one of ordinary skill in the art that the modeling process disclosed by Jonsson et al., which involves such statistical analyses as principal component analysis and partial least squares projections, is done using automatic devices, e.g. a computer.

The Pls1 and Pls2 are synthesized as oligonucleotides corresponding to the crossover sites according to the model (see page 737, "Oligomer synthesis"). These oligonucleotides bridge the crossover sites and therefore are bridging oligonucleotides, as required in the instant claims. To test the strength of Pls1 and Pls2, Jonsson et al. use several reference promoters, Pleon and Pa1, for comparison. The two promoters are generated through PCR amplification (see page 737, "PCR amplification of

reference promoters"). it would have been obvious to one of ordinary skill in the art to have understood that the PCR amplification process comprises synthesizing oligonucleotides, annealing or hybridizing them to parental nucleic acids, and elongating with a polymerase, as required in the instant claims. Although Jonsson et al. do not explicitly disclose PCR amplification of Pls1 and Pls2, it would have been obvious to one of ordinary skill in the art to have understood that this could have been done with a similar procedure as used for the PCR amplification of the reference promoters. Again, since the oligonucleotides bridge crossover sites, they are bridge oligonucleotides. The 25 parental promoter sequences disclosed by Jonsson et al. display low sequence similarity, as required in the instant claims, given the broad meaning of the term "low sequence similarity" (see page 734, Table 1). Josson et al. disclose selecting the recombinant Pls1 and Pls2 in silico after analyzing the structural features of each position of the 25 promoter sequences and determining the crossover sites(see pate 735, "Data analytical methods" and page 736, Figure 1). As stated above, the recombinant sequences Pls1 and Pls2 are selected by recombining the sites that contribute most to the overall promoter activity, obviously, the step of selecting crossover sites and the step of selecting the recombinant sequences occur simultaneously, as required in the instant claims, since selecting the crossover sites, i.e. sites that contribute most to the promoter activity, automatically results in the selection of the recombinant sequences.

The nucleic acid sequences disclosed by Josson et al. comprise homologous sequences, non-homologous sequences, artificial sequences, and sequences that correspond to naturally occurring nucleic acids, as required in the instant claims, since they comprise three categories: promoters from phage T5 and T2; promoters from phage lambda, and promoter of an artificial construct (see page 734, right column, first

paragraph, and Table 1). Josson et al. also disclose defining the structural and statistical criteria for the best promoter sequence comprising defining a structural or sequence based motif in the polynucleotide sequences to define the contribution of each position toward overall promoter activity (see page 736, Figures 1-3).

In summary, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the teachings and/or motivations of Josson et al. to simulate and produce recombinant nucleic acids or polypeptides in silico.

Conclusion

No claim is allowed.

Applicant is advised that the response to this requirement to be complete must include an affirmation of the provisional telephone election of the invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG

61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou: sjz
Patent Examiner
April 11, 2001

ARDIN H. MARSCHEL
PRIMARY EXAMINER